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<110> Mello, Craig C.  
Tabara, Hiroaki  
Grishok, Alla  
Fire, Andrew

<120> RNA INTERFERENCE PATHWAY GENES AS TOOLS FOR TARGETED GENETIC INTERFERENCE

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<150> US 60/193,218

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 Gly Ile Gly Arg Phe Glu Ile Ala Ala Thr Glu Ala Lys Asn Met Phe  
 595 600 605  
 Glu Arg Leu Pro Asp Lys Glu Gln Lys Val Leu Met Phe Ile Ile Ile  
 610 615 620  
 Ser Lys Arg Gln Leu Asn Ala Tyr Gly Phe Val Lys His Tyr Cys Asp  
 625 630 635 640  
 His Thr Ile Gly Val Ala Asn Gln His Ile Thr Ser Glu Thr Val Thr  
 645 650 655  
 Lys Ala Leu Ala Ser Leu Arg His Glu Lys Gly Ser Lys Arg Ile Phe  
 660 665 670  
 Tyr Gln Ile Ala Leu Lys Ile Asn Ala Lys Leu Gly Gly Ile Asn Gln  
 675 680 685  
 Glu Leu Asp Trp Ser Glu Ile Ala Glu Ile Ser Pro Glu Glu Lys Glu  
 690 695 700  
 Arg Arg Lys Thr Met Pro Leu Thr Met Tyr Val Gly Ile Asp Val Thr  
 705 710 715 720  
 His Pro Thr Ser Tyr Ser Gly Ile Asp Tyr Ser Ile Ala Ala Val Val  
 725 730 735  
 Ala Ser Ile Asn Pro Gly Gly Thr Ile Tyr Arg Asn Met Ile Val Thr  
 740 745 750  
 Gln Glu Glu Cys Arg Pro Gly Glu Arg Ala Val Ala His Gly Arg Glu  
 755 760 765  
 Arg Thr Asp Ile Leu Glu Ala Lys Phe Val Lys Leu Leu Arg Glu Phe  
 770 775 780  
 Ala Glu Asn Asn Asp Asn Arg Ala Pro Ala His Ile Val Val Tyr Arg  
 785 790 795 800  
 Asp Gly Val Ser Asp Ser Glu Met Leu Arg Val Ser His Asp Glu Leu  
 805 810 815  
 Arg Ser Leu Lys Ser Glu Val Lys Gln Phe Met Ser Glu Arg Asp Gly  
 820 825 830  
 Glu Asp Pro Glu Pro Lys Tyr Thr Phe Ile Val Ile Gln Lys Arg His  
 835 840 845

Asn	Thr	Arg	Leu	Leu	Arg	Arg	Met	Glu	Lys	Asp	Lys	Pro	Val	Val	Asn
850						855					860				
Lys	Asp	Leu	Thr	Pro	Ala	Glu	Thr	Asp	Val	Ala	Val	Ala	Ala	Val	Lys
865					870					875					880
Gln	Trp	Glu	Glu	Asp	Met	Lys	Glu	Ser	Lys	Glu	Thr	Gly	Ile	Val	Asn
				885					890					895	
Pro	Ser	Ser	Gly	Thr	Thr	Val	Asp	Lys	Leu	Ile	Val	Ser	Lys	Tyr	Lys
			900					905					910		
Phe	Asp	Phe	Phe	Leu	Ala	Ser	His	His	Gly	Val	Leu	Gly	Thr	Ser	Arg
	915						920					925			
Pro	Gly	His	Tyr	Thr	Val	Met	Tyr	Asp	Asp	Lys	Gly	Met	Ser	Gln	Asp
930						935					940				
Glu	Val	Tyr	Lys	Met	Thr	Tyr	Gly	Leu	Ala	Phe	Leu	Ser	Ala	Arg	Cys
945					950					955					960
Arg	Lys	Pro	Ile	Ser	Leu	Pro	Val	Pro	Val	His	Tyr	Ala	His	Leu	Ser
				965					970					975	
Cys	Glu	Lys	Ala	Lys	Glu	Leu	Tyr	Arg	Thr	Tyr	Lys	Glu	His	Tyr	Ile
			980					985					990		
Gly	Asp	Tyr	Ala	Gln	Pro	Arg	Thr	Arg	His	Glu	Met	Glu	His	Phe	Leu
	995					1000						1005			
Gln	Thr	Asn	Val	Lys	Tyr	Pro	Gly	Met	Ser	Phe	Ala				
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 <212> DNA  
 <213> Caenorhabditis elegans

<400> 4

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aagaaaactc	ccctcatggt	actagaagag	gctgctaagg	ctgtctatca	aaagacgcca	180
acttggggca	ctgtcgaact	tcttgaaggc	ttcgagatga	cgttgattct	gaatgaaatt	240
actgtaaaag	gccaggcaac	aagcaagaaa	gctgcgagac	aaaaggctgc	tgttgaatat	300
ttacgcaagg	ttgtggagaa	aggaaagcac	gaaatctttt	tcattcctgg	aacaaccaa	360
gaagaagctc	tttcgaatat	tgatcaaata	tcggataagg	ctgaggaatt	gaaacgatca	420
acttcagatg	ctgttcagga	taacgataac	gatgattcga	ttcctacaag	tgctgaattt	480
ccacctggta	tttcgccaac	cgagaattgg	gtcggaaagt	tgcaggaaaa	atctcaaaaa	540
agcaagctgc	aagccccaat	ctatgaagat	tccaagaatg	agagaaccga	gcgtttcttg	600
gttatatgca	cgatgtgcaa	tcaaaaaacc	agaggaatca	gaagtaagaa	gaaggacgca	660
aagaatcttg	cagcatgggt	gatgtggaaa	gcgttggaag	acggtatcga	atctctggaa	720
tcatatgata	tggttgatgt	gattgaaaat	ttggaagaag	ctgaacattt	actcgaaatt	780
caggatcaag	catccaagat	taaagacaag	cattccgcac	tgattgatat	actctcggac	840
aagaaaagat	tttcagacta	cagcatggat	ttcaacgtat	tatcagttag	cacaatggga	900
atacatcagg	tgctattgga	aatctcgttc	cggcgtctag	tttctccaga	ccccgacgat	960
ttggaaatgg	gagcagaaca	caccagact	gaagaaatta	tgaaggctac	tgccgagaag	1020
gaaaagctac	ggaagaagaa	tatgccagat	tccggggccgc	tagtgtttgc	tggacatggt	1080
tcatcggcgg	aagaggctaa	acagtgtgct	tgtaaatacgg	cgattatcca	tttcaacacc	1140
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 <213> Caenorhabditis elegans

<220>  
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 <223> Xaa = Any Amino Acid

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 Arg Thr Asp Leu Glu Met Phe Leu Lys Lys Thr Pro Leu Met Val Leu  
 35 40 45  
 Glu Glu Ala Ala Lys Ala Val Tyr Gln Lys Thr Pro Thr Trp Gly Thr  
 50 55 60  
 Val Glu Leu Pro Glu Gly Phe Glu Met Thr Leu Ile Leu Asn Glu Ile  
 65 70 75 80  
 Thr Val Lys Gly Gln Ala Thr Ser Lys Lys Ala Ala Arg Gln Lys Ala  
 85 90 95  
 Ala Val Glu Tyr Leu Arg Lys Val Val Glu Lys Gly Lys His Glu Ile  
 100 105 110  
 Phe Phe Ile Pro Gly Thr Thr Lys Glu Glu Ala Leu Ser Asn Ile Asp  
 115 120 125  
 Gln Ile Ser Asp Lys Ala Glu Glu Leu Lys Arg Ser Thr Ser Asp Ala  
 130 135 140  
 Val Gln Asp Asn Asp Asn Asp Asp Ser Ile Pro Thr Ser Ala Glu Phe  
 145 150 155 160  
 Pro Pro Gly Ile Ser Pro Thr Glu Asn Trp Val Gly Lys Leu Gln Glu  
 165 170 175  
 Lys Ser Gln Lys Ser Lys Leu Gln Ala Pro Ile Tyr Glu Asp Ser Lys  
 180 185 190  
 Asn Glu Arg Thr Glu Arg Phe Leu Val Ile Cys Thr Met Cys Asn Gln  
 195 200 205  
 Lys Thr Arg Gly Ile Arg Ser Lys Lys Lys Asp Ala Lys Asn Leu Ala  
 210 215 220  
 Ala Trp Leu Met Trp Lys Ala Leu Glu Asp Gly Ile Glu Ser Leu Glu  
 225 230 235 240  
 Ser Tyr Asp Met Val Asp Val Ile Glu Asn Leu Glu Glu Ala Glu His  
 245 250 255  
 Leu Leu Glu Ile Gln Asp Gln Ala Ser Lys Ile Lys Asp Lys His Ser  
 260 265 270  
 Ala Leu Ile Asp Ile Leu Ser Asp Lys Lys Arg Phe Ser Asp Tyr Ser  
 275 280 285  
 Met Asp Phe Asn Val Leu Ser Val Ser Thr Met Gly Ile His Gln Val  
 290 295 300  
 Leu Leu Glu Ile Ser Phe Arg Arg Leu Val Ser Pro Asp Pro Asp Asp  
 305 310 315 320  
 Leu Glu Met Gly Ala Glu His Thr Gln Thr Glu Glu Ile Met Lys Ala  
 325 330 335  
 Thr Ala Glu Lys Glu Lys Leu Arg Lys Lys Asn Met Pro Asp Ser Gly  
 340 345 350  
 Pro Leu Val Phe Ala Gly His Gly Ser Ser Ala Glu Glu Ala Lys Gln  
 355 360 365  
 Cys Ala Cys Lys Ser Ala Ile Ile His Phe Asn Thr Tyr Asp Phe Thr  
 370 375 380  
 Asp Xaa Lys Tyr Tyr Cys Val Phe Leu Lys Asn Glu Ala Ser Glu Xaa  
 385 390 395 400  
 Leu Xaa Lys Lys Lys Lys  
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 <211> 763  
 <212> PRT  
 <213> Arabidopsis thaliana

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 Gly Lys Arg Ala Asp Cys Pro Gln Glu Ala Val Gln Ile Leu Asp Ile  
 35 40 45  
 Val Leu Arg Glu Leu Ser Val Lys Arg Phe Cys Pro Val Gly Arg Ser  
 50 55 60  
 Phe Phe Ser Pro Asp Ile Lys Thr Pro Gln Arg Leu Gly Glu Gly Leu  
 65 70 75 80  
 Glu Ser Trp Cys Gly Phe Tyr Gln Ser Ile Arg Pro Thr Gln Met Gly  
 85 90 95  
 Leu Ser Leu Asn Ile Asp Met Ala Ser Ala Ala Phe Ile Glu Pro Leu  
 100 105 110  
 Pro Val Ile Glu Phe Val Ala Gln Leu Leu Gly Lys Asp Val Leu Ser  
 115 120 125  
 Lys Pro Leu Ser Asp Ser Asp Arg Val Lys Ile Lys Lys Gly Leu Arg  
 130 135 140  
 Gly Val Lys Val Glu Val Thr His Arg Ala Asn Val Arg Arg Lys Tyr  
 145 150 155 160  
 Arg Val Ala Gly Leu Thr Thr Gln Pro Thr Arg Glu Leu Met Phe Pro  
 165 170 175  
 Val Asp Glu Asn Cys Thr Met Lys Ser Val Ile Glu Tyr Phe Gln Glu  
 180 185 190  
 Met Tyr Gly Phe Thr Ile Gln His Thr His Leu Pro Cys Leu Gln Val  
 195 200 205  
 Gly Asn Gln Lys Lys Ala Ser Tyr Leu Pro Met Glu Ala Cys Lys Ile  
 210 215 220  
 Val Glu Gly Gln Arg Tyr Thr Lys Arg Leu Asn Glu Lys Gln Ile Thr  
 225 230 235 240  
 Ala Leu Leu Lys Val Thr Cys Gln Arg Ala Glu Gly Gln Arg Asn Asp  
 245 250 255  
 Ile Leu Arg Thr Val Gln His Asn Ala Tyr Asp Gln Asp Pro Tyr Ala  
 260 265 270  
 Lys Glu Phe Gly Met Asn Ile Ser Glu Lys Leu Ala Ser Val Glu Ala  
 275 280 285  
 Arg Ile Leu Pro Ala Pro Trp Leu Lys Tyr His Glu Asn Gly Lys Glu  
 290 295 300  
 Lys Asp Cys Leu Pro Gln Val Gly Gln Trp Asn Met Met Asn Lys Lys  
 305 310 315 320  
 Met Ile Asn Gly Met Thr Val Ser Arg Trp Ala Cys Val Asn Phe Ser  
 325 330 335  
 Arg Ser Val Gln Glu Asn Val Ala Arg Gly Phe Cys Asn Glu Leu Gly  
 340 345 350  
 Gln Met Cys Glu Val Ser Gly Met Glu Phe Asn Pro Glu Pro Val Ile  
 355 360 365  
 Pro Ile Tyr Ser Ala Arg Pro Asp Gln Val Glu Lys Ala Leu Lys His  
 370 375 380  
 Val Tyr His Thr Ser Met Asn Lys Thr Lys Gly Lys Glu Leu Glu Leu  
 385 390 395 400  
 Leu Leu Ala Ile Leu Pro Asp Asn Asn Gly Ser Leu Tyr Gly Asp Leu  
 405 410 415  
 Lys Arg Ile Cys Glu Thr Glu Leu Gly Leu Ile Ser Gln Cys Cys Leu  
 420 425 430  
 Thr Lys His Val Phe Lys Ile Ser Lys Gln Tyr Leu Ala Asp Val Ser  
 435 440 445  
 Leu Lys Ile Asn Val Lys Met Gly Gly Arg Asn Thr Val Leu Val Asp  
 450 455 460  
 Ala Ile Ser Cys Arg Ile Pro Leu Val Ser Asp Ile Pro Thr Ile Ile  
 465 470 475 480

Phe Gly Ala Asp Val Thr His Pro Glu Asn Gly Glu Glu Ser Ser Pro  
485 490 495  
Ser Ile Ala Ala Val Val Ala Ser Gln Asp Trp Pro Glu Val Thr Lys  
500 505 510  
Tyr Ala Gly Leu Val Cys Ala Gln Ala His Arg Gln Glu Leu Ile Gln  
515 520 525  
Asp Leu Tyr Lys Thr Trp Gln Asp Pro Val Arg Gly Thr Val Ser Gly  
530 535 540  
Gly Met Ile Arg Asp Leu Leu Ile Ser Phe Arg Lys Ala Thr Gly Gln  
545 550 555 560  
Lys Pro Leu Arg Ile Ile Phe Tyr Arg Asp Gly Val Ser Glu Gly Gln  
565 570 575  
Phe Tyr Gln Val Leu Leu Tyr Glu Leu Asp Ala Ile Arg Lys Ala Cys  
580 585 590  
Ala Ser Leu Glu Pro Asn Tyr Gln Pro Pro Val Thr Phe Ile Val Val  
595 600 605  
Gln Lys Arg His His Thr Arg Leu Phe Ala Asn Asn His Arg Asp Lys  
610 615 620  
Asn Ser Thr Asp Arg Ser Gly Asn Ile Leu Pro Gly Thr Val Val Asp  
625 630 635 640  
Thr Lys Ile Cys His Pro Thr Glu Phe Asp Phe Tyr Leu Cys Ser His  
645 650 655  
Ala Gly Ile Gln Gly Thr Ser Arg Pro Ala His Tyr His Val Leu Trp  
660 665 670  
Asp Glu Asn Asn Phe Thr Ala Asp Gly Ile Gln Ser Leu Thr Asn Asn  
675 680 685  
Leu Cys Tyr Thr Tyr Ala Arg Cys Thr Arg Ser Val Ser Ile Val Pro  
690 695 700  
Pro Ala Tyr Tyr Ala His Leu Ala Ala Phe Arg Ala Arg Phe Tyr Leu  
705 710 715 720  
Glu Pro Glu Ile Met Gln Asp Asn Gly Ser Pro Gly Lys Lys Asn Thr  
725 730 735  
Lys Thr Thr Thr Val Gly Asp Val Gly Val Lys Pro Leu Pro Ala Leu  
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<211> 678

<212> PRT

<213> *Drosophila melanogaster*

<400> 7

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Arg Ala Met Glu Gly Leu Asp Leu Lys Leu Val Ser Arg Tyr Tyr Tyr  
35 40 45  
Asp Pro Gln Ala Lys Ile Asn Leu Glu Asn Phe Arg Met Gln Leu Trp  
50 55 60  
Pro Gly Tyr Gln Thr Ser Ile Arg Gln His Glu Asn Asp Ile Leu Leu  
65 70 75 80  
Cys Ser Glu Ile Cys His Lys Val Met Arg Thr Glu Thr Leu Tyr Asn  
85 90 95  
Ile Leu Ser Asp Ala Ile Arg Asp Ser Asp Asp Tyr Gln Ser Thr Phe  
100 105 110  
Lys Arg Ala Val Met Gly Met Val Ile Leu Thr Asp Tyr Asn Asn Lys  
115 120 125  
Thr Tyr Arg Ile Asp Asp Val Asp Phe Gln Ser Thr Pro Leu Cys Lys  
130 135 140

Phe Lys Thr Asn Asp Gly Glu Ile Ser Tyr Val Asp Tyr Tyr Lys Lys  
 145 150 155 160  
 Arg Tyr Asn Ile Ile Arg Asp Leu Lys Gln Pro Leu Val Met Ser  
 165 170 175  
 Arg Pro Thr Asp Lys Asn Ile Arg Gly Gly Asn Asp Gln Ala Ile Met  
 180 185 190  
 Ile Ile Pro Glu Leu Ala Arg Ala Thr Gly Met Thr Asp Ala Met Arg  
 195 200 205  
 Ala Asp Phe Arg Thr Leu Arg Ala Met Ser Glu His Thr Arg Leu Asn  
 210 215 220  
 Pro Asp Arg Arg Ile Glu Arg Leu Arg Met Phe Asn Lys Arg Leu Lys  
 225 230 235 240  
 Ser Cys Lys Gln Ser Val Glu Thr Leu Lys Ser Trp Asn Ile Glu Leu  
 245 250 255  
 Asp Ser Ala Leu Val Glu Ile Pro Ala Arg Val Leu Pro Pro Glu Lys  
 260 265 270  
 Ile Leu Phe Gly Asn Gln Lys Ile Phe Val Cys Asp Ala Arg Ala Asp  
 275 280 285  
 Trp Thr Asn Glu Phe Arg Thr Cys Ser Met Phe Lys Asn Val His Ile  
 290 295 300  
 Asn Arg Trp Tyr Val Ile Thr Pro Ser Arg Asn Leu Arg Glu Thr Gln  
 305 310 315 320  
 Glu Phe Val Gln Met Cys Ile Arg Thr Ala Ser Ser Met Lys Met Asn  
 325 330 335  
 Ile Cys Asn Pro Ile Tyr Glu Glu Ile Pro Asp Asp Arg Asn Gly Thr  
 340 345 350  
 Tyr Ser Gln Ala Ile Asp Asn Ala Ala Ala Asn Asp Pro Gln Ile Val  
 355 360 365  
 Met Val Val Met Arg Ser Pro Asn Glu Glu Lys Tyr Ser Cys Ile Lys  
 370 375 380  
 Lys Arg Thr Cys Val Asp Arg Pro Val Pro Ser Gln Val Val Thr Leu  
 385 390 395 400  
 Lys Val Ile Ala Pro Arg Gln Gln Lys Pro Thr Gly Leu Met Ser Ile  
 405 410 415  
 Ala Thr Lys Val Val Ile Gln Met Asn Ala Lys Leu Met Gly Ala Pro  
 420 425 430  
 Trp Gln Val Val Ile Pro Leu His Gly Leu Met Thr Val Gly Phe Asp  
 435 440 445  
 Val Cys His Ser Pro Lys Asn Lys Asn Lys Ser Tyr Gly Ala Phe Val  
 450 455 460  
 Ala Thr Met Asp Gln Lys Glu Ser Phe Arg Tyr Phe Ser Thr Val Asn  
 465 470 475 480  
 Glu His Ile Lys Gly Gln Glu Leu Ser Glu Gln Met Ser Val Asn Met  
 485 490 495  
 Ala Cys Ala Leu Arg Ser Tyr Gln Glu Gln His Arg Ser Leu Pro Glu  
 500 505 510  
 Arg Ile Leu Phe Phe Arg Asp Gly Val Gly Asp Gly Gln Leu Tyr Gln  
 515 520 525  
 Val Val Asn Ser Glu Val Asn Thr Leu Lys Asp Arg Leu Asp Glu Ile  
 530 535 540  
 Tyr Lys Ser Ala Gly Lys Gln Glu Gly Cys Arg Met Thr Phe Ile Ile  
 545 550 555 560  
 Val Ser Lys Arg Ile Asn Ser Arg Tyr Phe Thr Gly His Arg Asn Pro  
 565 570 575  
 Val Pro Gly Thr Val Val Asp Asp Val Ile Thr Leu Pro Glu Arg Tyr  
 580 585 590  
 Asp Phe Phe Leu Val Ser Gln Ala Val Arg Ile Gly Thr Val Ser Pro  
 595 600 605  
 Thr Ser Tyr Asn Val Ile Ser Asp Asn Met Gly Leu Asn Ala Asp Lys  
 610 615 620

Leu Gln Met Leu Ser Tyr Lys Met Thr His Met Tyr Tyr Asn Tyr Ser  
 625 630 635 640  
 Gly Thr Ile Arg Val Pro Ala Val Cys His Tyr Ala His Lys Leu Ala  
 645 650 655  
 Phe Leu Val Ala Glu Ser Ile Asn Arg Ala Pro Ser Ala Gly Leu Gln  
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 Asn Gln Leu Tyr Phe Leu  
 675

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 <211> 69  
 <212> PRT  
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<220>  
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 <223> Xaa = Any Amino Acid

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 20 25 30  
 Xaa Phe Xaa Xaa Xaa Val Xaa Xaa Xaa Gly Xaa Xaa Xaa Xaa Gly  
 35 40 45  
 Xaa Gly Xaa Ser Lys Lys Xaa Xaa Ala Lys Xaa Xaa Ala Ala Xaa Xaa  
 50 55 60  
 Ala Leu Xaa Xaa Leu  
 65

<210> 9  
 <211> 766  
 <212> PRT  
 <213> Caenorhabditis elegans

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 20 25 30  
 Val Pro Phe Glu Ala Val Gln Ala Met Asp Val Ile Leu Arg His Leu  
 35 40 45  
 Pro Ser Leu Lys Tyr Thr Pro Val Gly Arg Ser Phe Phe Ser Pro Pro  
 50 55 60  
 Val Pro Asn Ala Ser Gly Val Met Ala Gly Ser Cys Pro Pro Gln Ala  
 65 70 75 80  
 Ser Gly Ala Val Ala Gly Gly Ala His Ser Ala Gly Gln Tyr His Ala  
 85 90 95  
 Glu Ser Lys Leu Gly Gly Gly Arg Glu Val Trp Phe Gly Phe His Gln  
 100 105 110  
 Ser Val Arg Pro Ser Gln Trp Lys Met Met Leu Asn Ile Asp Val Ser  
 115 120 125  
 Ala Thr Ala Phe Tyr Arg Ser Met Pro Val Ile Glu Phe Ile Ala Glu  
 130 135 140  
 Val Leu Glu Leu Pro Val Gln Ala Leu Ala Glu Arg Arg Ala Leu Ser  
 145 150 155 160  
 Asp Ala Gln Arg Val Lys Phe Thr Lys Glu Ile Arg Gly Leu Lys Ile  
 165 170 175

Glu Ile Thr His Cys Gly Gln Met Arg Arg Lys Tyr Arg Val Cys Asn  
 180 185 190  
 Val Thr Arg Arg Pro Ala Gln Thr Gln Thr Phe Pro Leu Gln Leu Glu  
 195 200 205  
 Thr Gly Gln Thr Ile Glu Cys Thr Val Ala Lys Tyr Phe Tyr Asp Lys  
 210 215 220  
 Tyr Arg Ile Gln Leu Lys Tyr Pro His Leu Pro Cys Leu Gln Val Gly  
 225 230 235 240  
 Gln Glu Gln Lys His Thr Tyr Leu Pro Pro Glu Val Cys Asn Ile Val  
 245 250 255  
 Pro Gly Gln Arg Cys Ile Lys Lys Leu Thr Asp Val Gln Thr Ser Thr  
 260 265 270  
 Met Ile Lys Ala Thr Ala Arg Ser Ala Pro Glu Arg Glu Arg Glu Ile  
 275 280 285  
 Ser Asn Leu Val Arg Lys Ala Glu Phe Ser Ala Asp Pro Phe Ala His  
 290 295 300  
 Glu Phe Gly Ile Thr Ile Asn Pro Ala Met Thr Glu Val Lys Gly Arg  
 305 310 315 320  
 Val Leu Ser Ala Pro Lys Leu Leu Tyr Gly Gly Arg Thr Arg Ala Thr  
 325 330 335  
 Ala Leu Pro Asn Gln Gly Val Trp Asp Met Arg Gly Lys Gln Phe His  
 340 345 350  
 Thr Gly Ile Asp Val Arg Val Trp Ala Ile Ala Cys Phe Ala Gln Gln  
 355 360 365  
 Gln His Val Lys Glu Asn Asp Leu Arg Met Phe Thr Asn Gln Leu Gln  
 370 375 380  
 Arg Ile Ser Asn Asp Ala Gly Met Pro Ile Val Gly Asn Pro Cys Phe  
 385 390 395 400  
 Cys Lys Tyr Ala Val Gly Val Glu Gln Val Glu Pro Met Phe Lys Tyr  
 405 410 415  
 Leu Lys Gln Asn Tyr Ser Gly Ile Gln Leu Val Val Val Val Leu Pro  
 420 425 430  
 Gly Lys Thr Pro Val Tyr Ala Glu Val Lys Arg Val Gly Asp Thr Val  
 435 440 445  
 Leu Gly Ile Ala Thr Gln Cys Val Gln Ala Lys Asn Ala Ile Arg Thr  
 450 455 460  
 Thr Pro Gln Thr Leu Ser Asn Leu Cys Leu Lys Met Asn Val Lys Leu  
 465 470 475 480  
 Gly Gly Val Asn Ser Ile Leu Leu Pro Asn Val Arg Pro Arg Ile Phe  
 485 490 495  
 Asn Glu Pro Val Ile Phe Phe Gly Cys Asp Ile Thr His Pro Pro Ala  
 500 505 510  
 Gly Asp Ser Arg Lys Pro Ser Ile Ala Ala Val Val Gly Ser Met Asp  
 515 520 525  
 Ala His Pro Ser Arg Tyr Ala Ala Thr Val Arg Val Gln Gln His Arg  
 530 535 540  
 Gln Glu Ile Ile Ser Asp Leu Thr Tyr Met Val Arg Glu Leu Leu Val  
 545 550 555 560  
 Gln Phe Tyr Arg Asn Thr Arg Phe Lys Pro Ala Arg Ile Val Val Tyr  
 565 570 575  
 Arg Asp Gly Val Ser Glu Gly Gln Phe Phe Asn Val Leu Gln Tyr Glu  
 580 585 590  
 Leu Arg Ala Ile Arg Glu Ala Cys Met Met Leu Glu Arg Gly Tyr Gln  
 595 600 605  
 Pro Gly Ile Thr Phe Ile Ala Val Gln Lys Arg His His Thr Arg Leu  
 610 615 620  
 Phe Ala Val Asp Lys Lys Asp Gln Val Gly Lys Ala Tyr Asn Ile Pro  
 625 630 635 640  
 Pro Gly Thr Thr Val Asp Val Gly Ile Thr His Pro Thr Glu Phe Asp  
 645 650 655

Phe Tyr Leu Cys Ser His Ala Gly Ile Gln Gly Thr Ser Arg Pro Ser  
660 665 670  
His Tyr His Val Leu Trp Asp Asp Asn Asn Leu Thr Ala Asp Glu Leu  
675 680 685  
Gln Gln Leu Thr Tyr Gln Met Cys His Thr Tyr Val Arg Cys Thr Arg  
690 695 700  
Ser Val Ser Ile Pro Ala Pro Ala Tyr Tyr Ala His Leu Val Ala Phe  
705 710 715 720  
Arg Ala Arg Tyr His Leu Val Asp Arg Glu His Asp Ser Gly Glu Gly  
725 730 735  
Ser Gln Pro Ser Gly Thr Ser Glu Asp Thr Thr Leu Ser Asn Met Ala  
740 745 750  
Arg Ala Val Gln Val Ile Leu Ala Phe Asn Leu Val Ser Ile  
755 760 765

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<211> 737  
<212> PRT  
<213> Oryctolagus cuniculus

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20 25 30  
Pro Phe Glu Thr Ile Gln Ala Leu Asp Val Val Met Arg His Leu Pro  
35 40 45  
Ser Met Arg Tyr Thr Pro Val Gly Arg Ser Phe Phe Thr Ala Ser Glu  
50 55 60  
Gly Cys Ser Asn Pro Leu Gly Gly Gly Arg Glu Val Trp Phe Gly Phe  
65 70 75 80  
His Gln Ser Val Arg Pro Ser Leu Trp Lys Met Met Leu Asn Ile Asp  
85 90 95  
Val Ser Ala Thr Ala Phe Tyr Lys Ala Gln Pro Val Ile Glu Phe Val  
100 105 110  
Cys Glu Val Leu Asp Phe Lys Ser Ile Glu Glu Gln Gln Lys Pro Leu  
115 120 125  
Thr Asp Ser Gln Arg Val Lys Phe Thr Lys Glu Ile Lys Gly Leu Lys  
130 135 140  
Val Glu Ile Thr His Cys Gly Gln Met Lys Arg Lys Tyr Arg Val Cys  
145 150 155 160  
Asn Val Thr Arg Arg Pro Ala Ser His Gln Thr Phe Pro Leu Gln Gln  
165 170 175  
Glu Ser Gly Gln Thr Val Glu Cys Thr Val Ala Gln Tyr Phe Lys Asp  
180 185 190  
Arg His Lys Leu Val Leu Arg Tyr Pro His Leu Pro Cys Leu Gln Val  
195 200 205  
Gly Gln Glu Gln Lys His Thr Tyr Leu Pro Leu Glu Val Cys Asn Ile  
210 215 220  
Val Ala Gly Gln Arg Cys Ile Lys Lys Leu Thr Asp Asn Gln Thr Ser  
225 230 235 240  
Thr Met Ile Arg Ala Thr Ala Arg Ser Ala Pro Asp Arg Gln Glu Glu  
245 250 255  
Ile Ser Lys Leu Met Arg Ser Ala Ser Phe Asn Thr Asp Pro Tyr Val  
260 265 270  
Arg Glu Phe Gly Ile Met Val Lys Asp Glu Met Thr Asp Val Thr Gly  
275 280 285  
Arg Val Leu Gln Pro Pro Ser Ile Leu Tyr Gly Gly Arg Asn Lys Ala  
290 295 300  
Ile Ala Thr Pro Val Gln Gly Val Trp Asp Met Arg Asn Lys Gln Phe  
305 310 315 320

His Thr Gly Ile Glu Ile Lys Val Trp Ala Ile Ala Cys Phe Ala Pro  
 325 330 335  
 Gln Arg Gln Cys Thr Glu Val His Leu Lys Ser Phe Thr Glu Gln Leu  
 340 345 350  
 Arg Lys Ile Ser Arg Asp Ala Gly Met Pro Ile Gln Gly Gln Pro Cys  
 355 360 365  
 Phe Cys Lys Tyr Ala Gln Gly Ala Asp Ser Val Gly Pro Met Phe Arg  
 370 375 380  
 His Leu Lys Asn Thr Tyr Ala Gly Leu Gln Leu Val Val Val Ile Leu  
 385 390 395 400  
 Pro Gly Lys Thr Pro Val Tyr Ala Glu Val Lys Arg Val Gly Asp Thr  
 405 410 415  
 Val Leu Gly Met Ala Thr Gln Cys Val Gln Met Lys Asn Val Gln Arg  
 420 425 430  
 Thr Thr Pro Gln Thr Leu Ser Asn Leu Cys Leu Lys Ile Asn Val Lys  
 435 440 445  
 Leu Gly Gly Val Asn Asn Ile Leu Leu Pro Gln Gly Arg Pro Pro Val  
 450 455 460  
 Phe Gln Gln Pro Val Ile Phe Leu Gly Ala Asp Val Thr His Pro Pro  
 465 470 475 480  
 Ala Gly Asp Gly Lys Lys Pro Ser Ile Ala Ala Val Val Gly Ser Met  
 485 490 495  
 Asp Ala His Pro Asn Arg Tyr Cys Ala Thr Val Arg Val Gln Gln His  
 500 505 510  
 Arg Gln Glu Ile Ile Gln Asp Leu Ala Ala Met Val Arg Glu Leu Leu  
 515 520 525  
 Ile Gln Phe Tyr Lys Ser Thr Arg Phe Lys Pro Thr Arg Ile Ile Phe  
 530 535 540  
 Tyr Arg Asp Gly Val Ser Glu Gly Gln Phe Gln Gln Val Leu His His  
 545 550 555 560  
 Glu Leu Leu Ala Ile Arg Glu Ala Cys Ile Lys Leu Glu Lys Asp Tyr  
 565 570 575  
 Gln Pro Gly Ile Thr Phe Ile Val Val Gln Lys Arg His His Thr Arg  
 580 585 590  
 Leu Phe Cys Thr Asp Lys Asn Glu Arg Val Gly Lys Ser Gly Asn Ile  
 595 600 605  
 Pro Ala Gly Thr Thr Val Asp Thr Lys Ile Thr His Pro Thr Glu Phe  
 610 615 620  
 Asp Phe Tyr Leu Cys Ser His Ala Gly Ile Gln Gly Thr Ser Arg Pro  
 625 630 635 640  
 Ser His Tyr His Val Leu Trp Asp Asp Asn Arg Phe Ser Ser Asp Glu  
 645 650 655  
 Leu Gln Ile Leu Thr Tyr Gln Leu Cys His Thr Tyr Val Arg Cys Thr  
 660 665 670  
 Arg Ser Val Ser Ile Pro Ala Pro Ala Tyr Tyr Ala His Leu Val Ala  
 675 680 685  
 Phe Arg Ala Arg Tyr His Leu Val Asp Lys Glu His Asp Ser Ala Glu  
 690 695 700  
 Gly Ser His Thr Ser Gly Gln Ser Asn Gly Arg Asp His Gln Ala Leu  
 705 710 715 720  
 Ala Lys Ala Val Gln Val His Gln Asp Thr Leu Arg Thr Met Tyr Phe  
 725 730 735  
 Ala

<210> 11  
 <211> 66  
 <212> PRT  
 <213> Xenopus laevis

<400> 11

Pro Val Gly Ser Leu Gln Glu Leu Ala Val Gln Lys Gly Trp Arg Leu  
 1 5 10 15  
 Pro Glu Tyr Thr Val Ala Gln Glu Ser Gly Pro Pro His Lys Arg Glu  
 20 25 30  
 Phe Thr Ile Thr Cys Arg Val Glu Thr Phe Val Glu Thr Gly Ser Gly  
 35 40 45  
 Thr Ser Lys Gln Val Ala Lys Arg Val Ala Ala Glu Lys Leu Leu Thr  
 50 55 60  
 Lys Phe  
 65

<210> 12

<211> 66

<212> PRT

<213> Homo sapiens

<400> 12

Phe Met Glu Glu Leu Asn Thr Tyr Arg Gln Lys Gln Gly Val Val Leu  
 1 5 10 15  
 Lys Tyr Gln Glu Leu Pro Asn Ser Gly Pro Pro His Asp Arg Arg Phe  
 20 25 30  
 Thr Phe Gln Val Ile Ile Asp Gly Arg Glu Phe Pro Glu Gly Glu Gly  
 35 40 45  
 Arg Ser Lys Lys Glu Ala Lys Asn Ala Ala Ala Lys Leu Ala Val Glu  
 50 55 60  
 Ile Leu  
 65

<210> 13

<211> 818

<212> PRT

<213> Caenorhabditis elegans

<400> 13

Val Asn Glu Glu Ile Lys Val Gln Phe Ala Lys Asn Phe Val Tyr Asp  
 1 5 10 15  
 Asn Asn Ser Ile Leu Arg Val Pro Glu Ser Phe His Asp Pro Asn Arg  
 20 25 30  
 Phe Glu Gln Ser Leu Glu Val Ala Pro Arg Ile Glu Ala Trp Phe Gly  
 35 40 45  
 Ile Tyr Ile Gly Ile Lys Glu Leu Phe Asp Gly Glu Pro Val Leu Asn  
 50 55 60  
 Phe Ala Ile Val Asp Lys Leu Phe Tyr Asn Ala Pro Lys Met Ser Leu  
 65 70 75 80  
 Leu Asp Tyr Leu Leu Leu Ile Val Asp Pro Gln Ser Cys Asn Asp Asp  
 85 90 95  
 Val Arg Lys Asp Leu Lys Thr Lys Leu Met Ala Gly Lys Met Thr Ile  
 100 105 110  
 Arg Gln Ala Ala Arg Pro Arg Ile Arg Gln Leu Leu Glu Asn Leu Lys  
 115 120 125  
 Leu Lys Cys Ala Glu Val Trp Asp Asn Glu Met Ser Arg Leu Thr Glu  
 130 135 140  
 Arg His Leu Thr Phe Leu Asp Leu Cys Glu Glu Asn Ser Leu Val Tyr  
 145 150 155 160  
 Lys Val Thr Gly Lys Ser Asp Arg Gly Arg Asn Ala Lys Lys Tyr Asp  
 165 170 175  
 Thr Thr Leu Phe Lys Ile Tyr Glu Glu Asn Lys Lys Phe Ile Glu Phe  
 180 185 190  
 Pro His Leu Pro Leu Val Lys Val Lys Ser Gly Ala Lys Glu Tyr Ala  
 195 200 205

Val Pro Met Glu His Leu Glu Val His Glu Lys Pro Gln Arg Tyr Lys  
210 215 220  
Asn Arg Ile Asp Leu Val Met Gln Asp Lys Phe Leu Lys Arg Ala Thr  
225 230 235 240  
Arg Lys Pro His Asp Tyr Lys Glu Asn Thr Leu Lys Met Leu Lys Glu  
245 250 255  
Leu Asp Phe Ser Ser Glu Glu Leu Asn Phe Val Glu Arg Phe Gly Leu  
260 265 270  
Cys Ser Lys Leu Gln Met Ile Glu Cys Pro Gly Lys Val Leu Lys Glu  
275 280 285  
Pro Met Leu Val Asn Ser Val Asn Glu Gln Ile Lys Met Thr Pro Val  
290 295 300  
Ile Arg Gly Phe Gln Glu Lys Gln Leu Asn Val Val Pro Glu Lys Glu  
305 310 315 320  
Leu Cys Cys Ala Val Phe Val Val Asn Glu Thr Ala Gly Asn Pro Cys  
325 330 335  
Leu Glu Glu Asn Asp Val Val Lys Phe Tyr Thr Glu Leu Ile Gly Gly  
340 345 350  
Cys Lys Phe Arg Gly Ile Arg Ile Gly Ala Asn Glu Asn Arg Gly Ala  
355 360 365  
Gln Ser Ile Met Tyr Asp Ala Thr Lys Asn Glu Tyr Ala Phe Tyr Lys  
370 375 380  
Asn Cys Thr Leu Asn Thr Gly Ile Gly Arg Phe Glu Ile Ala Ala Thr  
385 390 395 400  
Glu Ala Lys Asn Met Phe Glu Arg Leu Pro Asp Lys Glu Gln Lys Val  
405 410 415  
Leu Met Phe Ile Ile Ile Ser Lys Arg Gln Leu Asn Ala Tyr Gly Phe  
420 425 430  
Val Lys His Tyr Cys Asp His Thr Ile Gly Val Ala Asn Gln His Ile  
435 440 445  
Thr Ser Glu Thr Val Thr Lys Ala Leu Ala Ser Leu Arg His Glu Lys  
450 455 460  
Gly Ser Lys Arg Ile Phe Tyr Gln Ile Ala Leu Lys Ile Asn Ala Lys  
465 470 475 480  
Leu Gly Gly Ile Asn Gln Glu Leu Asp Trp Ser Glu Ile Ala Glu Ile  
485 490 495  
Ser Pro Glu Glu Lys Glu Arg Arg Lys Thr Met Pro Leu Thr Met Tyr  
500 505 510  
Val Gly Ile Asp Val Thr His Pro Thr Ser Tyr Ser Gly Ile Asp Tyr  
515 520 525  
Ser Ile Ala Ala Val Val Ala Ser Ile Asn Pro Gly Gly Thr Ile Tyr  
530 535 540  
Arg Asn Met Ile Val Thr Gln Glu Glu Cys Arg Pro Gly Glu Arg Ala  
545 550 555 560  
Val Ala His Gly Arg Glu Arg Thr Asp Ile Leu Glu Ala Lys Phe Val  
565 570 575  
Lys Leu Leu Arg Glu Phe Ala Glu Asn Asn Asp Asn Arg Ala Pro Ala  
580 585 590  
His Ile Val Val Tyr Arg Asp Gly Val Ser Asp Ser Glu Met Leu Arg  
595 600 605  
Val Ser His Asp Glu Leu Arg Ser Leu Lys Ser Glu Val Lys Gln Phe  
610 615 620  
Met Ser Glu Arg Asp Gly Glu Asp Pro Glu Pro Lys Tyr Thr Phe Ile  
625 630 635 640  
Val Ile Gln Lys Arg His Asn Thr Arg Leu Leu Arg Arg Met Glu Lys  
645 650 655  
Asp Lys Pro Val Val Asn Lys Asp Leu Thr Pro Ala Glu Thr Asp Val  
660 665 670  
Ala Val Ala Val Lys Gln Trp Glu Glu Asp Met Lys Glu Ser Lys  
675 680 685

Glu Thr Gly Ile Val Asn Pro Ser Ser Gly Thr Thr Val Asp Lys Leu  
690 695 700  
Ile Val Ser Lys Tyr Lys Phe Asp Phe Phe Leu Ala Ser His His Gly  
705 710 715 720  
Val Leu Gly Thr Ser Arg Pro Gly His Tyr Thr Val Met Tyr Asp Asp  
725 730 735  
Lys Gly Met Ser Gln Asp Glu Val Tyr Lys Met Thr Tyr Gly Leu Ala  
740 745 750  
Phe Leu Ser Ala Arg Cys Arg Lys Pro Ile Ser Leu Pro Val Pro Val  
755 760 765  
His Tyr Ala His Leu Ser Cys Glu Lys Ala Lys Glu Leu Tyr Arg Thr  
770 775 780  
Tyr Lys Glu His Tyr Ile Gly Asp Tyr Ala Gln Pro Arg Thr Arg His  
785 790 795 800  
Glu Met Glu His Phe Leu Gln Thr Asn Val Lys Tyr Pro Gly Met Ser  
805 810 815  
Phe Ala

<210> 14

<211> 63

<212> PRT

<213> Caenorhabditis elegans

<400> 14

Trp Val Gly Lys Leu Gln Phe Lys Ser Gln Lys Ser Lys Leu Gln Ala  
1 5 10 15  
Asp Ile Tyr Glu Asp Ser Lys Asn Glu Arg Thr Glu Phe Thr Leu Val  
20 25 30  
Ile Cys Thr Met Cys Asn Gln Lys Thr Arg Gly Ile Thr Ser Lys Gln  
35 40 45  
Lys Asp Ala Lys Asn Leu Ala Ala Trp Leu Met Trp Lys Ala Leu  
50 55 60